REMARKS

Claims 49, 57, 58 and 79 were pending in the subject application, with claims 1-48, 50-56 and 59-78 having previously been canceled, without prejudice or disclaimer. By this Amendment, claims 49, 57, 58 and 79 have been amended to clarify the claimed subject matter, and new claims 80 and 81 have been added. Claims 49, 57, 58 and 79-81 would be pending upon entry of this amendment, with claim 49 being the sole pending claim in independent form.

Support for the claim amendments can be found in the application as originally filed, for example, at page 11, line 34 through page 12, line 6, page 19, lines 3-7, page 23, line 23 through page 24, line 32, page 31, lines 8-12, page 33, lines 1-25, and page 34, line 34 through page 35, line 19, and in Fig. 9.

Accordingly, Applicant respectfully requests that this Amendment be entered.

Rejection under 35 U.S.C. §112, first paragraph

In section 3 of the April 20, 2010 Office Action, claims 49, 57, 58 and 79 were rejected under 35 U.S.C. § 112, first paragraph, as allegedly failing to comply with the written description requirement.

In response, without conceding the correctness of the Examiner's position but solely to advance the prosecution of the subject application, The claims have been amended to address the formal issue referenced in the Office Action.

Withdrawal of the rejection under 35 U.S.C. § 112, first paragraph, is respectfully requested.

Rejections Under 35 U.S.C. § 103(a)

In section 5 of the April 20, 2010 final Office Action, claims 49, 57, 58 and 79 were rejected under 35 U.S.C. § 103(a) as allegedly unpatentable over Hollis et al. (US 5,846,708) in view of Dattagupta (US 4,777,129) or Wang et al. (US 4,925,785).

Applicant respectfully submits that the present application is allowable over the cited art, for at least the reason that the cited art does not disclose or suggest the aspects of the present application of a method for analyzing a sample oligonucleotide sequence including ***providing a permeation layer adjacent to a micro-electrode in each of the microscopic locations, said permeation layer having selective diffusion properties thereby permitting the free transport of counter-ions to said micro-electrode and inhibiting large binding entities from physical contact with said micro-electrode***.

As discussed in the present application (see, for example, page 24, lines 16-20), the use of a permeation layer allows electrolysis reactions required for electrophoretic transport to occur on the micro-electrode surface, but avoids adverse electrochemical effects to the binding entities, reactants and analytes.

Hollis, as understood by applicant, proposes a microelectronic sensor array for RNA and DNA sequencing, as shown in Figure 1 (reproduced below) of Hollis, wherein the sequencer 10 includes an X-Y array of test sites 12 electronically addressable by conductive leads X1, X2, … XN on the X-axis and conductive leads Y1, Y2, … YN on the Y-axis. The test sites 12 are formed in a semiconductor wafer using semiconductor photolithographic processing techniques.

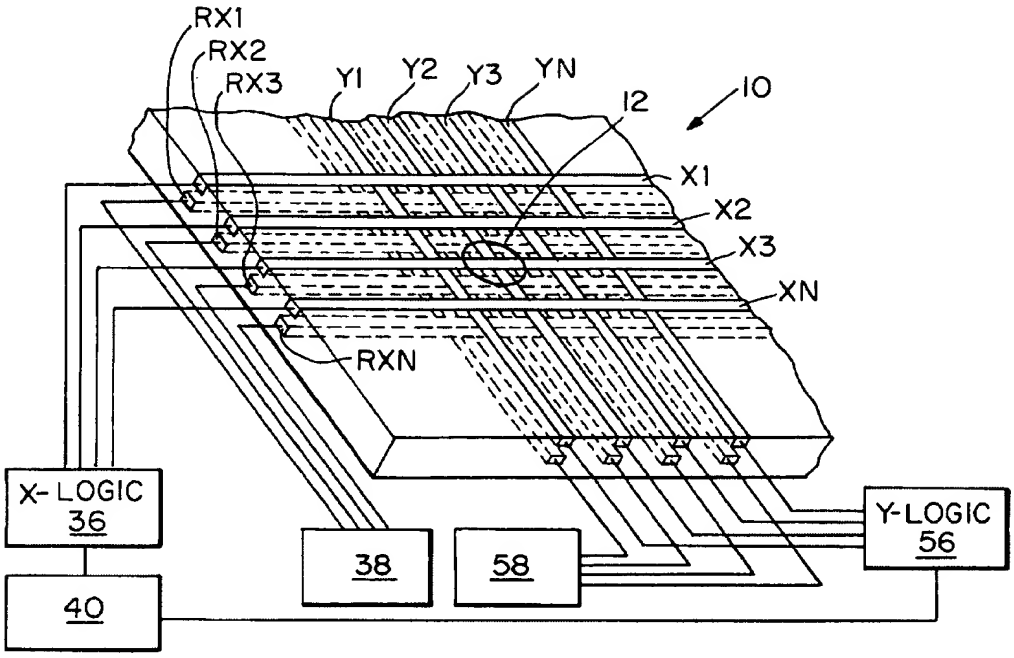

Fig. 1

Each test site contains a plurality of probes 22, as illustrated in Fig. 4 (reproduced below) of Hollis, which are capable of binding to known molecular structures or "targets" (for example, polynucleotides, DNA, RNA, cells, antibodies or anti-antibodies).

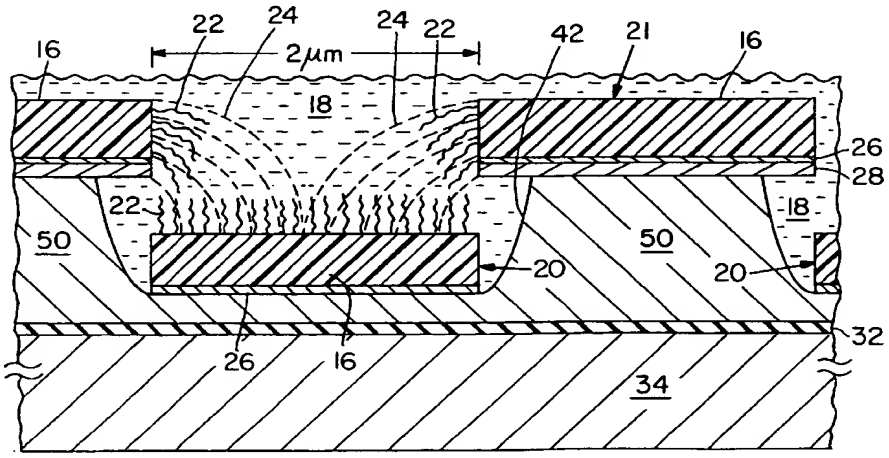

Fig. 4

The probes 22 are formed on electrodes 16 and 20 in Hollis, and when a sample substance containing the targets in an electrolyte solution 18 is poured onto array 10, the targets bind with associated probes 22 within a plurality of wells 42 formed in each test site 12.

Hollis proposes various possible coatings for electrodes in an alternative embodiment (Fig. 15 of Hollis), the main function of which appears to be protection of the charge-coupled device (CCD) from degradation due to exposure to aqueous solution (see, for example, col. 9, lines 20-27 of Hollis).

However, in sharp contrast to the method of the present application, Hollis does NOT disclose or suggest the need for a layer providing selective permeability.

Additionally, Hollis proposes some possibilities for attachment of probes, including, for example, the functionalizing of a glass surface with epoxy silane, as to allow covalent binding of oligonucleotides (see, for example, Hollis, col. 11, lines 1-41).

However, Hollis simply does NOT in any way teach or suggest the possibility of using a permeation layer with selective permeability to allow certain chemicals to reach the electrode while blocking others.

Hollis, as understood by applicant, uses electrodes in a hybridization process to *detect* hybridization (see examples of Hollis), rather than actively control the hybridization process.

However, applicant submits Hollis does not teach or suggest using charge to control hybridization, and in addition, Hollis is also silent regarding the aforementioned aspects of providing a

permeation layer as recited in claim 49 of the present application.

Dattagupta, as understood by applicant, proposes labeled mobile probes each complementary to a target DNA sequence that is further complementary to an immobilized capture probe.

Wang, as understood by applicant, proposes mobile probes and target molecules in solution applied to immobilized capture probes forming sandwich complexes.

However, Dattagupta and Wang, like Hollis, do NOT disclose or suggest use of electrodes to control hybridization, and likewise do NOT disclose or suggest providing a permeation layer as recited in amended claim 49 of the present application.

Applicant submits that the cited art, even when considered along with common sense and common knowledge to one skilled in the art, does ***NOT*** render unpatentable the aforementioned aspects of the present application.

Accordingly, applicant submits that amended claim 49 and the claims depending therefrom are allowable over the cited art.

Withdrawal of the rejection under 35 U.S.C. § 103 is requested.

Nonstatutory Obviousness-type Double Patenting Rejection

In section 7 of the April 20, 2010 final Office Action, claims 49, 57, 58 and 79 were rejected on the ground of nonstaturtory obviousness-type double patenting as purportedly unpatentable over claims 1-12 of U.S. Patent No. 6,051,380 in view of Dattagupta or Douglas (US 5,556,748).

Claims 1-12 of U.S. Patent No. 6,051,380 are reproduced below:

1. A method for transport and hybridization of DNA in an active electronic system comprising the steps of:

providing a low conductivity, zwitterionic buffer on said device,

electrophoretically transporting said nucleic acid towards a microlocation,

applying current and voltage to the microlocation to effect transportation, whereby the local pH above the microlocation is below the pH of the buffer at its isoelectric point, whereby hybridization between the nucleic acid and a probe located at the microlocation is enhanced.

2. The method for enhanced transport and hybridization of nucleic acids of claim 1, wherein the low conductivity, zwitterionic buffer is histidine.

3. The method for enhanced transport and hybridization of nucleic acids of claim 1, wherein the low conductivity, zwitterionic buffer is L-histidine.

4. The method for enhanced transport and hybridization of nucleic acids of claim 1, wherein the low conductivity, zwitterionic buffer is D-histidine.

5. A method for the effective transport and hybridization of DNA on an active, electronic matrix device, the device having a plurality of microlocations, at least certain of the microlocations including probes, comprising the steps of:

providing a first low-conductivity, zwitterionic buffer to the device,

providing said nucleic acids to the device in said low conductivity, zwitterionic buffer,

applying current and potential to at least certain microlocations so as to effect transport of said nucleic acids to selected microlocations,

changing the buffer to a second buffer with a high salt concentration, and

effecting hybridization of said nucleic acid with said probe at selected microlocations.

6. The method for effecting transport and hybridization of nucleic acids of claim 5, wherein the low conductivity, zwitterionic buffer is cysteine.

7. The method for effecting transport and

hybridization of nucleic acids of claim 5, wherein the low conductivity, zwitterionic buffer is alanine.

8. The method for effecting transport and hybridization of nucleic acids of claim 5, wherein the salt concentration is from approximately 50 mM to 100 mM.

9. A method for detection of point mutations in double stranded amplicons comprising the steps of:
providing amplicon products to an active, programmable electronic matrix device,
dilute said products in a low conductance histidine buffer,
denature said products,
hybridize said denatured products in the histidine buffer on the device,
perform stringency so as to discriminate matches versus mismatches, and
detect and analyze said products.

10. The method of claim 9 for detecting point mutations in amplicons wherein the stringency includes electronic stringency.

11. The method of claim 9 for detecting point mutations in amplicons wherein the detection is fluorescent detection.

12. The method of claim 9 for detecting point mutations in amplicons wherein a fluorescent reporter probe sequence is hybridized with said product.

Applicant respectfully points out that none of claims 1-12 of U.S. Patent No. 6,051,380, nor Dattagupta and Douglas, discloses or suggests the aforementioned aspects of ***providing a permeation layer adjacent to a micro-electrode in each of said microscopic locations, said permeation layer having selective diffusion properties thereby permitting the free transport of counter-ions to said micro-electrode and inhibiting large binding entities from physical contact with said micro-electrode***.

Accordingly, withdrawal of the obviousness-type double patenting rejection is requested.

In view of the amendments to the claims and remarks hereinabove, applicant submits that the application is allowable. Applicant earnestly solicits the allowance of the application.

If a petition for a further extension of time is required to make this response timely, this paper should be considered to be such a petition.

The Patent Office is hereby authorized to charge any additional required fees, and to credit any overpayment during prosecution of this application, to our Deposit Account No. 03-3125.

If a telephone interview could advance the prosecution of this application, the Examiner is respectfully requested to call the undersigned attorney.

Respectfully submitted,

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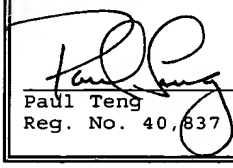
I hereby certify that this correspondence is being deposited this date with the U.S. Postal Service with sufficient postage as first class mail in an envelope addressed to: Mail Stop RCE, Commissioner for Patents, P.O. Box 1450, Alexandria, VA 22313-1450.



August 12, 2010

Paul Teng
Reg. No. 40,837

Date